

1. (original) A mutant of a protein, the protein causing a disease after having performed a conformational transition, the disease comprising:
 - a) neurodegenerative diseases of the group comprising Transmissible Spongiform Encephalopathy (TSE), Alzheimers disease, Multiple Sclerosis, and Parkinsons disease; and/or other
 - b) conformational diseases of the group comprising Primary systematic amyloidosis, Type II diabetes, and Atrial amyloidosis;wherein the mutant protein or a variant of which comprises at least one additional engineered disulfide bond which inhibits a conformational transition of such proteins in human and animals.
2. (original) The protein of claim 1,
wherein the at least one additional disulfide bond is engineered at a position similar to a disulfide bond in a structurally related non-pathogenic protein.
3. (original) The protein of claim 1,
wherein the protein is a prion protein, the at least one engineered additional disulfide bond being situated in the globular domain.
4. (original) The prion protein of claim 3,
wherein the at least one engineered additional disulfide bond is situated in a position similar as in the doppel protein (Dpl).
5. (original) The prion protein of claim 3,
wherein the protein comprises a 'factor X' binding epitope and the at least one engineered additional disulfide bond is situated within this 'factor X' binding epitope.
6. (original) The prion protein of claim 3,
wherein the at least one engineered additional disulfide bond is introduced between a first segment comprising the amino acid residues 165-175 and a second

segment comprising the C-terminal amino acid residues 215-230 in a human prion protein or between structurally corresponding amino acid segments in other species.

7. (original) The prion protein of claim 6,
wherein the at least one engineered additional disulfide bond is linking amino acid residues M166C and E221C or amino acid residues M166C and Y225C.
8. (original) A nucleic acid sequence coding for a mutant protein, the protein causing a disease after having performed a conformational transition, the disease comprising:
 - a) neurodegenerative diseases of the group comprising Transmissible Spongiform Encephalopathy (TSE), Alzheimers disease, Multiple Sclerosis, and Parkinsons disease; and/or other
 - b) conformational diseases of the group comprising Primary systematic amyloidosis, Type II diabetes, and Atrial amyloidosis;wherein the nucleic acid sequence is coding for the mutant protein or a variant of which that comprises at least one additional engineered disulfide bond which inhibits a conformational transition of such proteins in human and animals.
9. (original) Plasmid constructs, vectors, transformed cells, transgenic animals including cattle, sheep, cat, elk, and deer, and recombinant proteins, comprising and/or being encoded by a nucleic acid sequence according to claim 8.
10. (original) Use of a mutant of a protein, the protein causing a disease after having performed a conformational transition, the disease comprising:
 - a) neurodegenerative diseases of the group comprising Transmissible Spongiform Encephalopathy (TSE), Alzheimers disease, Multiple Sclerosis, and Parkinsons disease; and/or other
 - b) conformational diseases of the group comprising Primary systematic amyloidosis, Type II diabetes, and Atrial amyloidosis;

the mutant protein or a variant of which comprising at least one additional engineered disulfide bond which inhibits a conformational transition of such proteins in human and/or animals, wherein the mutant protein is used for therapeutic treatment of conformational diseases.

11. (original) Use of a mutant of a protein, the protein causing a disease after having performed a conformational transition, the disease comprising:

- a) neurodegenerative diseases of the group comprising Transmissible Spongiform Encephalopathy (TSE), Alzheimers disease, Multiple Sclerosis, and Parkinsons disease; and/or other
- b) conformational diseases of the group comprising Primary systematic amyloidosis, Type II diabetes, and Atrial amyloidosis;

the mutant protein or a variant of which comprising at least one additional engineered disulfide bond which inhibits a conformational transition of such proteins in human and/or animals, wherein the mutant protein is used for the manufacturing of a medicament for the therapeutic treatment of conformational diseases.

12. (currently amended) The use according to claim 10 ~~or 11~~,

wherein the engineered additional disulfide bond(s) prevent(s) a conformational transition of mutant PrP^C into PrP^{Sc} and thus suppress(es) a conformational transition of mutant PrP^C into PrP^{Sc} in co-existing wild-type proteins by dominant negative inhibition.

13. (currently amended) The use according to claim 10 ~~or 11~~,

wherein the conformational transition of wild type PrP^C into PrP^{Sc} oligomers is suppressed by binding of mutant PrP^C to wild-type PrP^C.

14. (currently amended) The use according to claim 10 ~~or 11~~,

wherein the conformational transition of wild type PrP^{Sc} oligomers into PrP^{Sc} amyloid fibrils is suppressed by binding of mutant PrP^C to wild-type PrP^{Sc} oligomers.

15. (currently amended) The use according to claim 10 ~~or 11~~,
wherein the conformational transition of wild type PrP^C into PrP^C/PrP^{Sc} heterodimers is suppressed by binding of mutant PrP^C to wild-type PrP^{Sc}.
16. (currently amended) The use according to claim 10 ~~or 11~~,
wherein the elongation of amyloid fibrils or the dissociation of amyloid fibrils into PrP^{Sc} oligomers is suppressed by binding of mutant PrP^C to wild-type PrP^{Sc} amyloid fibrils.
17. (currently amended) The use according to claim 8, 9, 10, ~~or 11~~,
wherein *in vivo* generation of disulfide mutants of prion proteins or variants thereof is carried out in order to enable an intended therapy of Transmissible Spongiform Encephalopathy (TSE) in human, e.g. by somatic gene therapy with lentiviral vector, where TSE includes spontaneous, in herited, iatrogenic and variant forms of Creutzfeldt-Jakob disease (CJD), fatal familial insomnia (FFI), and Gerstmann-Sträussler-Scheinker syndrome (GSS).
18. (currently amended) The use according to claim 10 ~~or 11~~,
wherein the recombinant production of disulfide mutants of prion proteins or variants thereof is carried out in order to enable an intended therapy of TSE in human, e.g. by direct application of the recombinant protein, where TSE includes spontaneous, inherited, iatrogenic and variant forms of CJD, FFI, and GSS.
19. (currently amended) The use according to claim 8, 9, 10, ~~or 11~~,
wherein *in vivo* generation of disulfide mutants of prion proteins or variants thereof is carried out in order to enable an intended therapy of TSE in animals, e.g. by somatic gene therapy with lentiviral vector, where TSE includes bovine

spongiform encephalopathy (BSE), scrapie in sheep, feline spongiform encephalopathy (FSE), and chronic wasting disease (CWD) in elk and deer.

20. (currently amended) The use according to claim 10 ~~or 11~~,
wherein recombinant production of disulfide mutants of prion proteins or variants thereof is carried out in order to enable an intended therapy of TSE in animals, e.g. by direct application of the recombinant protein, where TSE includes BSE, scrapie, FSE and CWD.
21. (currently amended) The use according to claim 10 ~~or 11~~,
wherein recombinant production of disulfide mutants of prion proteins or variants thereof is carried out as “conversion-resistant PrP^C standard” for TSE-tests applied to human or animals, where recombinant PrP^C is amplified by PrP^{Sc} from pathogenic tissue or bodily fluid such as blood and urine.
22. (currently amended) The use according to claim 10 ~~or 11~~,
wherein *in vivo* generation of disulfide mutants of prion proteins or variants thereof is carried out in order to enable breeding of TSE-resistant animals by somatic gene therapy with lentiviral vector, where animals include cattle, sheep, cat, elk, deer, pig, horse, and fish.
23. (original) Medicament for the treatment of:
- a) neurodegenerative diseases of the group comprising Transmissible Spongiform Encephalopathy (TSE), Alzheimers disease, Multiple Sclerosis, and Parkinsons disease; and/or other
 - b) conformational diseases of the group comprising Primary systematic amyloidosis, Type II diabetes, and Atrial amyloidosis;
- in humans, the medicament comprising a mutant protein or a variant of which comprising at least one additional engineered disulfide bond which inhibits a conformational transition of such proteins.

24. (original) Medicament for the treatment of bovine spongiform encephalopathy (BSE), scrapie in sheep, feline spongiform encephalopathy (FSE), and chronic wasting disease (CWD) in elk and deer, the medicament comprising a mutant protein or a variant of which comprising at least one additional engineered disulfide bond which inhibits a conformational transition of such proteins.